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CITIZEN PETITION

Kirkpatrick & Lockhart, LLP ("petitioner"), on behalf of a pharmaceutical client, hereby submits this citizen petition ("petition") pursuant to section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act ("the Act"), and its implementing regulations. 21 U.S.C.§§ 355(j)(2)(C) (1994); 21 C.F.R. §§ 10.25, 10.30, 314.93 (2001). This petition requests that the Commissioner of Food and Drugs ("the Commissioner") permit the filing of an abbreviated new drug application ("ANDA") for a methotrexate sodium oral solution, 5 mg/mL.

A. Action Requested

The petitioner requests authorization from the Commissioner to submit an ANDA for a methotrexate oral solution, 5 mg/mL. The proposed drug product differs from the listed drug, Lederle Pharmaceutical Division of American Cyanamid Company's ("Lederle's") methotrexate sodium tablets (eq 2.5 mg base), only in dosage form as permitted by section 505(j)(2)(C) of the Act. 21 U.S.C. § 355(j)(2)(C).

B. Statement of Grounds

The Act provides, in relevant part, that any person may file an ANDA for the approval of a new drug that is the "same" as a listed drug. 21 U.S.C. § 355(j)(2)(A), (j)(6); 21 C.F.R. § 314.92(a)(1). Abbreviated applications also may be submitted for a new drug, which differs from a listed drug in one or more specified aspects, provided that FDA has declared the product suitable for ANDA submission through the petition process. 21 U.S.C. § 355(j)(2)(A), (j)(2)(C); 21 C.F.R. § 314.92(a)(3). Permitted product changes include, among other things, a different route of administration, dosage form, or strength from that of a listed drug. Id. FDA must approve a petition seeking one or more of these product changes, unless the proposed product change(s) presents questions of safety or effectiveness. 21 U.S.C. § 355 (j)(2)(C)(i); 21 C.F.R. § 314.93.

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This petition accordingly seeks FDA authorization to submit an ANDA for a methotrexate sodium oral solution, 5 mg/mL product. The proposed ANDA will reference the listed drug, methotrexate sodium tablets, 2.5 mg, which is manufactured by Lederle. The proposed drug product will differ from the listed drug in strength and dosage form -- changes that are permitted by the Act. Specifically, the proposed product will contain the same active ingredient for the same labeled use as the reference listed drug, but as a solution rather than a tablet dosage form and in 5 mg/mL strength. Please note that higher strengths of methotrexate sodium tablets, 5 mg, 7.5 mg, 10 mg and 15 mg have been approved by the Agency and are being marketed. Although methotrexate sodium tablets, 15 mg is also a listed drug, our client decided to base this petition on the 2.5 mg strength to avoid unnecessary exposure of healthy subjects to a high dose of methotrexate during the biostudy. Further, the innovator has conducted pediatric studies in support of their indication for juvenile rheumatoid arthritis, and the labeling for the listed drug contains the appropriate pediatric information. Therefore, the safety of methotrexate sodium in pediatric patients has been established.

The availability of the oral solution dosage form will improve overall patient compliance and the unique dispensing method will minimize the patient's physical contact with this potentially toxic product. The proposed oral solution drug product has been designed to be easily dosed without the need to crush tablets for patients who have difficulty swallowing tablets. In addition, the solution will be administered via a special dosing device that minimizes physical contact with the product. Thus, the proposed drug product will provide physicians with an additional dosage option for ease of administration, while providing the same therapeutic and safety benefits as that of the listed drug. In addition, the proposed drug should improve patient compliance because the need for additional compounding will be eliminated.

The labeling of the proposed drug product will be the same as the currently approved labeling for the listed drug, with a few minor changes which are required because of differences approved under this petition; i.e., dosage form. See Attachments. In order to limit the volume of drug that may be administered, and to avoid excessive intake of propylene glycol, a statement has been added in the "Dosage and Administration" section limiting the daily dosage to no more than 12mL. This statement was added to address concerns regarding the total intake of propylene glycol and the Office of Generic Drug's suggestion to limit propylene glycol intake to 6 g per day. In light of the above, and the fact that methotrexate sodium has been marketed in the U.S. for many years, there is no reason to question the safety or efficacy of the proposed methotrexate sodium oral solution product for its intended uses.

C. Environmental Impact

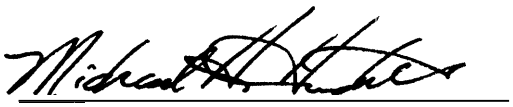
Petitioner claims a categorical exclusion under 21 C.F.R. § 25.31 (2001).

D. Economic Impact

Information under this section will be submitted upon request by the Commissioner.

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views upon which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.



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Attachments:

1. Electronic Orange Book, Approved Drug Products with Therapeutic Equivalence Evaluations, updated as of April 26, 2002, Lederle's methotrexate sodium tablets.
2. Copy of the package insert for Lederle's methotrexate sodium tablets.
3. Proposed package insert for methotrexate sodium oral solution, 5 mg/mL.